



Attorney Docket No.: 126387.120

PATENT

IFW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Initial Application of: :
D. Lynn Kirkpatrick et al. :
Serial No. 10/617,949 : Group Art Unit: 1614
Filed: July 10, 2003 : Examiner: not yet assigned
For: ASYMMETRIC DISULFIDES AND METHODS OF USING SAME

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In accordance with the provisions of 37 C.F.R. 1.56, 1.97 and 1.98, the attention of the Patent and Trademark Office is hereby directed to the documents listed on the attached form PTO-1449. Copies are provided. It is respectfully requested that the documents be expressly considered and that the documents be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

It is respectfully requested that the references be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.



AUTHORIZATION

No fee is required. The Commissioner is hereby authorized to charge any additional fees which may be required for this submission, or credit any overpayment to deposit account no. 50-0436.

Respectfully submitted,

PEPPER HAMILTON LLP

Raymond A. Miller
Registration No. 42,891

Pepper Hamilton LLP
One Mellon Bank Center
50th Floor
500 Grant Street
Pittsburgh, PA 15219
Telephone: (412) 454-5813
Facsimile: (412) 281-0717
Date: May 27, 2004



<p>Substitute for form 1449/PTO</p> <p>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p> <p>(use as many sheets as necessary)</p>				Complete if Known	
				Application Number	10/617,949
				Filing Date	July 10, 2003
				First Named Inventor	Kirkpatrick
				Group Art Unit	1614
				Examiner Name	not yet assigned
Sheet	1	of 3		Attorney Docket Number	126387.120

U.S. PATENT DOCUMENTS

Examiner's Initials	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code (if known)			
		6,552,060	B1	Kirkpatrick	04-22-2003	
		4,149,003	B1	Carlsson	04-10-1979	
		4,188,488	B1	Dubs	02-12-1980	
		5,338,542	B1	Thorpe	08-16-1994	
		5,416,064	B1	Chari	05-16-1995	
		5,475,092	B1	Chari	12-12-1995	
		5,633,274	B1	Halperin	05-27-1997	
		5,645,988	B1	Vande Woude	07-08-1997	
		5,756,068	B1	Jimbow	05-26-1998	

FOREIGN PATENT DOCUMENTS

Examiner's Initials	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
		Office	Number	Kind Code (if known)				
		WO	98/00160		National Jewish Center	01-08-98		
		WO	98/24472		Powis	06-11-98		
		WO	98/29449		Incyte Pharmaceuticals, Inc.	07-09-98		
		WO	91/04320		Aktibolaget, Astra	04-04-1991		

OTHER ART (Including Author, Title, Date, Pertinent Pages, Etc.)

Examiner's Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or county where published.	T
		Krohne-Enrich G. et al. Glutathione Reductase from Human Erythrocytes. Isolation of the Enzyme and sequence analysis of the redox-active peptide. Eur. J. Biochem. 80 (1971): 65-71.	
		Grippo, J.F. et al. Evidence that the Endogenous Heat-Stable Glucocorticoid Receptor-Activating Factor is Thioredoxin. J. Biol. Chem. 258 (1983): 13658-64.	
		Holmgren, A. et al. Thioredoxin. Ann. Rev. Biochem. 54 (1985): 237-71.	
		Kirkpatrick, D.L. Modification of Antitumor Disulfide cytotoxicity by Glutathione Depletion. Cancer Res. 47 (1987): 4391-95.	
		Silverman, R.B. et al. Reduced Thioredoxin: A Possible Physiological Cofactor for Vitamin K Epoxide Reductase. Further Support for an Active Site Disulfide. Biochem. Biophys. Res. Commun. 155 (1988): 1248-54.	
		Boyd, M.R. Status of Implementation of the NCI Human Tumor Cell in Line in vitro Primary Drug Screen. Proc Am. Assoc. Cancer Res. 30 (1989): 652-54.	
		Coshan-Gauthier, R. et al. Modulation of Disulfide Antitumor Activity in Balb/c mice through Glutathione Depletion. Exp. Cell Biol. 57 (1989): 273-80.	
		Cromlish, J.A. et al. Human Transcription Factor IIIC (TFIIC). Purification, Polypeptide Structure, and the Involvement of Thiol Groups in Specific DNA Binding. J. Biol. Chem. 264 (1989): 18100-109.	
		Kirkpatrick, D.L. Kinetic Studies of the Interaction of Glutathione with Four Antitumor Disulfides: Possible Mechanism for cellular GSH depletion. Chem. Biol. Interact. 69 (1989): 225-34.	

<p>Substitute for form 1449/PTO</p> <p>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p> <p>(use as many sheets as necessary)</p>				Complete if Known	
				Application Number	10/617,949
				Filing Date	July 10, 2003
				First Named Inventor	Kirkpatrick
				Group Art Unit	1614
				Examiner Name	not yet assigned
Sheet	2	of 3		Attorney Docket Number	126387.120
<p>Kirkpatrick, D.L. et al. Inhibitory Effect of Cytotoxic Disulfides on membrane Na+/K+ ATPase. Biochem. Pharmacol. 39 (1990): 1484-87.</p> <p>Lundstrom, J. et al. Protein Disulfide-isomerase is a Substrate for Thioredoxin reductase and has Thioredoxin-like Activity. J.Biol. Chem. 265 (1990): 9114-20.</p> <p>Wakasugi, N. et al. Adult T-Cell Leukemia derived factor/thioredoxin produced by both human T-lymphotropic Virus Type 1 and Epstein-Barr virus-transformed lymphocytes, acts as an autocrine growth factor and synergized with interleukin-1 and interleukin-2. Proc. Natl. Acad. Sci. USA 87 (1990): 8282-86.</p> <p>Fujii, S. et al. Coexpression of Adult T-Cell Leukemia-derived factor, a Human Thioredoxin Homologue, and Human Papillomavirus DNA in Neoplastic Cervical Squamous Epithelium. Cancer 68 (1991): 1583-91.</p> <p>Yodoi, J. et al. ADF a Growth-Promoting Factor Derived from Adult T-Cell Leukemia and Homologous to Thioredoxin: Involvement in Lymphocyte Immortalization by HTLV-1 and EBV. Adv. Cancer Res. 57 (1991): 381-411.</p> <p>Ericson, M.L. et al. Secretion of Thioredoxin After in vitro Activation of Human B Cells. Lymphokine Cytokine Res. 11 (1992): 201-07.</p> <p>Fountoulakis, M. et al. Unfolding Intermediates of the Extracellular Domain of the Interferon Gamma Receptor. J. Biol. Chem. 267 (1992): 7095-7100.</p> <p>Kirkpatrick, D.L. et al. Effect of a Hypoxic Tumor Cell Cytotoxic Disulfide on the Membrane and DNA of Tumor Cells in Culture. Anticancer Drugs 3 (1992): 651-58.</p> <p>Kirkpatrick, D.L. et al. Synthesis and Evaluation of Imidazolyl Disulfides for Selective Cytotoxicity to Hypoxic EMT6 Tumor Cells in vitro. Euro. J. Med. Chem. 27 (1992): 33-37.</p> <p>Matthews, J.R. et al. Thioredoxin Regulates the DNA Binding Activity of NF-KappaB by Reduction of a Disulphide Bond Involving Cysteine 62. Nucleic Acids Res. 20 (1992): 3821-30.</p> <p>Nakamura, H. et al. Expression and Growth-Promoting Effect of Adult T-Cell Leukemia-derived Factor. A Human Thioredoxin Homologue in Hepatocellular Carcinoma. Cancer 69 (1992): 2091-97.</p> <p>Paull, K.D. et al. Identification of Novel Antimitotic Agents acting at the Tubulin Level by Computer-Assisted Evaluation of Differential Cytotoxicity Data. Cancer Res. 52 (1992): 3892-3900.</p> <p>Gasdaska, J.R. et al. Cell Growth Stimulation by the Redox Protein Thioredoxin Occurs by a Novel Helper Mechanism. Cell Growth Differ. 6 (1995): 1642-50.</p> <p>Baker, A., et al.: "Thioredoxin, a gene found overexpressed in human cancer" Cancer Research 57(22):5162-5167 (1997)</p> <p>Kuperus, M. et al. Interaction of Redox Active Disulfides with the Autocrine Growth Factor, Human Thioredoxin. Proc. Am. Assoc. Cancer Res. 36 (1995): 2541.</p> <p>Orr, A. et al. "Waterbug" Dialysis. Biotechniques 19 (1995): 204-206.</p> <p>Rubartelli, A. et al. High Rates of Thioredoxin Secretion Correlate with Growth Arrest in Hepatoma Cells. Cancer Res. 55 (1995): 675-80.</p> <p>Powis, G., et al.: "Selenium and the Thioredoxin Redox System" Oncology Research 9(6-7):303-312 (1997).</p> <p>Borman, S. Combinatorial Chemists Focus on Small Molecules, Molecular Recognition and Automation. Chem. Eng. News 74 (1996): 29-54.</p> <p>Gallegos, A., et al.: "Transfection with human thioredoxin increases cell proliferation and a dominant-negative mutant thioredoxin reverses the transformed phenotype of human breast cancer cells" Cancer Research 56(24): 5765-5770 (1996).</p> <p>Gasdaska, J.R. et al. Oxidative Inactivation of Thioredoxin as a Cellular Growth Factor and Protection by CYS(73) – Ser Mutation. Biochem. Pharmacol. 52 (1996): 1741-47.</p> <p>Gladyshev, V.N. et al. Selenocysteine, Identified as the Penultimate C-Terminal Residue in Human T-Cell Thioredoxin Reductase, Corresponds to TGA in the Human Placental Gene. Proc. Natl. Acad. Sci USA 93 (1996): 6146-47.</p> <p>Rubartelli, A. et al. Secretion of Thioredoxin by Normal and Neoplastic Cells Through a Leaderless Secretory Pathway. J. Biol. Chem. 267/34 (Dec. 5, 1992): 24161-64.</p> <p>Hayashi, T. Oxidoreductive Regulation of Nuclear Factor KappaB: Involvement of a Cellular Reducing Catalyst Thioredoxin. J. Biol. Chem. 268 (1993): 11380-388.</p> <p>Oblong, J.E. et al. Purification of Human Thioredoxin Reductase: Properties and Characterization by Absorption and Circular Dichroism Spectroscopy. Biochemistry 32 (1993): 7271-77.</p> <p>Wang, Y. et al. Wild-type p53-triggered apoptosis is inhibited by bcl-2 in a v-myc-induced T-Cell Lymphoma Line. Oncogene 8 (1993): 3427-31.</p>					

<p>Substitute for form 1449/PTO</p> <p>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p> <p>(use as many sheets as necessary)</p>				Complete if Known	
				Application Number	10/617,949
				Filing Date	July 10, 2003
				First Named Inventor	Kirkpatrick
				Group Art Unit	1614
				Examiner Name	not yet assigned
Sheet	3	of 3		Attorney Docket Number	126387.120
		Galter, D. et al. Distinct Effects of Glutathione Disulfide on the Nuclear Transcription Factors KappaB and the Activator Protein-1. <i>Eur. J. Biochem.</i> 221 (1994): 639-48.			
		Gasdaska, P.Y. et al. The Predicted Amino Acid Sequence of Human Thioredoxin is identical to that of the Autocrine Growth Factor Human Adult T-Cell Derived Factor (ADF): Thioredoxin mRNA is Elevated in Some Human Tumors. <i>Biochem. Biophys. Acta</i> 1218 (1994): 292-96.			
		Kirkpatrick, D.L. et al. Disulfide Cytotoxicity Under Hypoxia. <i>Oncol. Res.</i> 6/10-11 (1994): 545-52.			
		Oblong, J.E. et al. Site-directed Mutagenesis of Active Site Cysteines in Human Thioredoxin Produces Competitive Inhibitors of Human Thioredoxin Reductase and Elimination of Mitogenic Properties of Thioredoxin. <i>J. Biol. Chem.</i> 269 (1994): 11714-720.			
		Oblong, J.E. et al. Reversible Inhibition of Human Thioredoxin Reductase Activity by Cytotoxic Alkyl 2-imidazolyl Disulfide Analogues. <i>Cancer Chem. Pharmacol.</i> 34 (1994): 434-38.			
		Powis, G. et al. The thioredoxin/Thioredoxin Reductase Redox System and Control of Cell Growth. <i>Oncol. Res.</i> 6/10-11 (1994): 539-44.			
		Verentchikov, A.N. et al. Reflecting time-of-flight mass spectrometer with an electrospray ion source and orthogonal extraction. <i>Anal. Chem.</i> 66 (1994): 126-133.			
		Berggren, M., et al.: "Thioredoxin and Thioredoxin Reductase Gene Expression in Human Tumors and Cell Lines" <i>Anticancer Research</i> 16:3459-3466, XP002062159 (Nov.-Dec. 1996).			
		Weichsel, A. et al. Crystal Structures of Reduced, Oxidized and Mutated Human Thioredoxins: Evidence for a Regulatory Homodimer. <i>Structure</i> 4 (1996): 735-751.			
		Kirkpatrick, D.L. et al. Antitumor Activity of Inhibitors of a Novel Signaling Pathway: Thioredoxin/Thioredoxin Reductase. <i>Proc. Am. Assoc. Cancer Res.</i> 38 (1997): 4115.			
		Kirkpatrick, D.L. et al. Redox Control as a Target for Anticancer Drug Development. <i>Current Pharmaceutical Design</i> 3 (1997): 305-22.			
		Kirkpatrick, D.L. et al. Redox Active Disulfides: The Thioredoxin System as a Drug Target. <i>Oncology Research</i> 9 (1997): 351-56.			
		Kunkel, M.W. et al. Cell Line-Directed Screening Assay for Inhibitors of Thioredoxin Reductase Signaling as Potential Anti-Cancer Drugs. <i>Anti-Cancer Drug Design</i> 12 (1997) 659-70.			
		Kirkpatrick, D.L. et al. Mechanisms of Inhibition of the Thioredoxin Growth Factor System by Antitumor 2-Imidazolyl Disulfides. <i>Biochemical Pharmacology</i> 55 (1998): 987-94.			
		Tockman, et al.: <i>Cancer Research</i> (Suppl) 52: 2715-2718 (1992).			
		Gura: <i>Science</i> 278: 1041-1045 (1997)			
		Jain: <i>Sci. Am.</i> 271:58-65 (1994)			
		Hartwell, et al: <i>Science</i> : 278: 1064-1068 (1997)			
		Kirkpatrick, D.L., et al., "Stimulation of Apoptosis by a Redox Active Disulfide" <i>Proc. Am. Association, Cancer Res.</i> 36 (1995): 2541			
		Drexler, et al. Leukemia and Lymphoma, 9:1-25 (1993)			
		Embleton, et al.: <i>Immunol. Ser.</i> 23:181-207 (1984)			
		Curti, et al.; <i>Crit. Rev. in Oncology/Hematology</i> , 14:29-39 (1993)			
		Mustafa O., et al.: <i>International Journal of Oncology</i> , 8(5):883-888 (1996)			
		Freshney: <i>Culture of Animal Cells, a Manual of Basic Technique</i> , Alan R. Liss, Inc., Pg. 4 (1983)			
		Powis, G., et al.: Thioredoxin Redox Signalling: a Novel Target for Anti-Cancer Drug Development, <i>Anti-Cancer Drugs</i> , 7:121-126 (1996)			
		Mau, B.L., et al.: <i>Biochem. Pharmacol.</i> , 43: 1613-1620 (1992)			
		Schallreuter, K.U. , <i>Biochem Biophys Acta</i> , 1504: 14-20 (1990)			
Examiner Signature				Date Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.10

APPLICANT: D. Lynn Kirkpatrick et al.

TITLE: ASYMMETRIC DISULFIDES AND METHODS OF USING SAME

SERIAL NO. 10/617,949

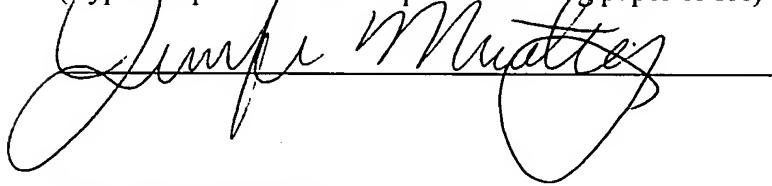
ATTORNEY REF: 126387.120

DATE OF DEPOSIT: May 27, 2004

I HEREBY CERTIFY THAT THIS INFORMATION DISCLOSURE STATEMENT WITH COPIES OF REFERENCES CITED THEREIN IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE VIA FIRST CLASS MAIL UNDER 37 CFR 1.10 ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO COMMISSIONER FOR PATENTS, MAIL STOP ASSIGNMENT, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450.

Jennifer Martinez

(Typed or printed name of person mailing paper or fee)



Documents Enclosed:

1. Information Disclosure Statement with cited references;
2. Certificate of Mailing;
3. Postcard